Temple University
College of Engineering

Bimodal Imaging of Breast Cancer using Profile Diagrams and Convolution Neural Network

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Motivation

- American Cancer Society estimates that in 2021 in the United States
  - 300,000 women will be diagnosed with **invasive breast cancer**,
  - additional 50,000 with **non-invasive (in-situ) breast cancer**,
  - and about 45,000 women will **die** from breast cancer
  - **Inflammatory Breast Cancer affects a small population but deadly**
- While there are many advanced technologies for breast cancer detection, women from remote, rural, or underdeveloped communities have **limited access** to cancer screening
- There is a **need for an inexpensive and easy-to-use breast cancer identification device**.

Outline

- Background and Research Goals
- Bimodal Imaging: Tactile Imaging Probe
  - Tactile Profile Diagrams
  - Tactile Properties using CNN classification
- Bimodal Imaging: Multispectral Imaging Probe
  - Multispectral Profile Diagrams
  - Spectral Properties using CNN classification
- Breast cancer risk assessment
  - Multimodal Index
- Conclusions

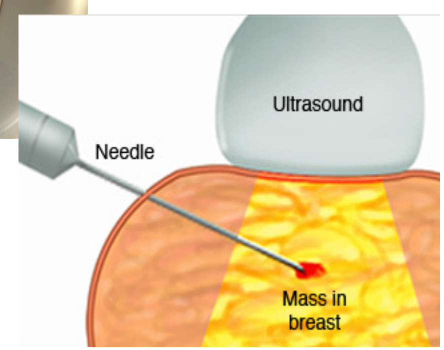
Background

Mammography
- powerful screening method
- x-ray radiation
- high number of false positives

Ultrasound
- can show certain breast changes
- low spatial resolution
- low sensitivity

Magnetic Resonance Imaging (MRI)
- used for detailed examination
- costly
- limited specificity

Biopsy
- gold standard to confirm BC
- highly invasive
- cancerous tumors are sometimes missed



Background

- Breast cancer are often detected through **breast lumps**; however, in more rare cases such as IBC, **breast tissue changes without an underlying tumor**.

- Our breast cancer detection and characterization methods aim to quantify **tumor stiffness** or tissue **breast tissue physiologic changes.**

- Cancerous tumors are **stiffer** than benign lesions
  - **Tactile sensors** characterize tumor stiffness, location, and size
  - Most tactile sensors are electromechanical pressure sensors

- Breast tissue **optical properties** change when the tissue becomes malignant (angiogenesis and hypermetabolic activity)
  - **Hyperspectral/multispectral imaging** can characterize superficial optical properties of suspicious breast tissues
  - Hyperspectral imaging is available, yet **costly and time consuming**.

Research Goals

The primary goal of this research is to develop a **bimodal imaging system for breast tumor and tissue characterization** using tactile and multispectral imaging.

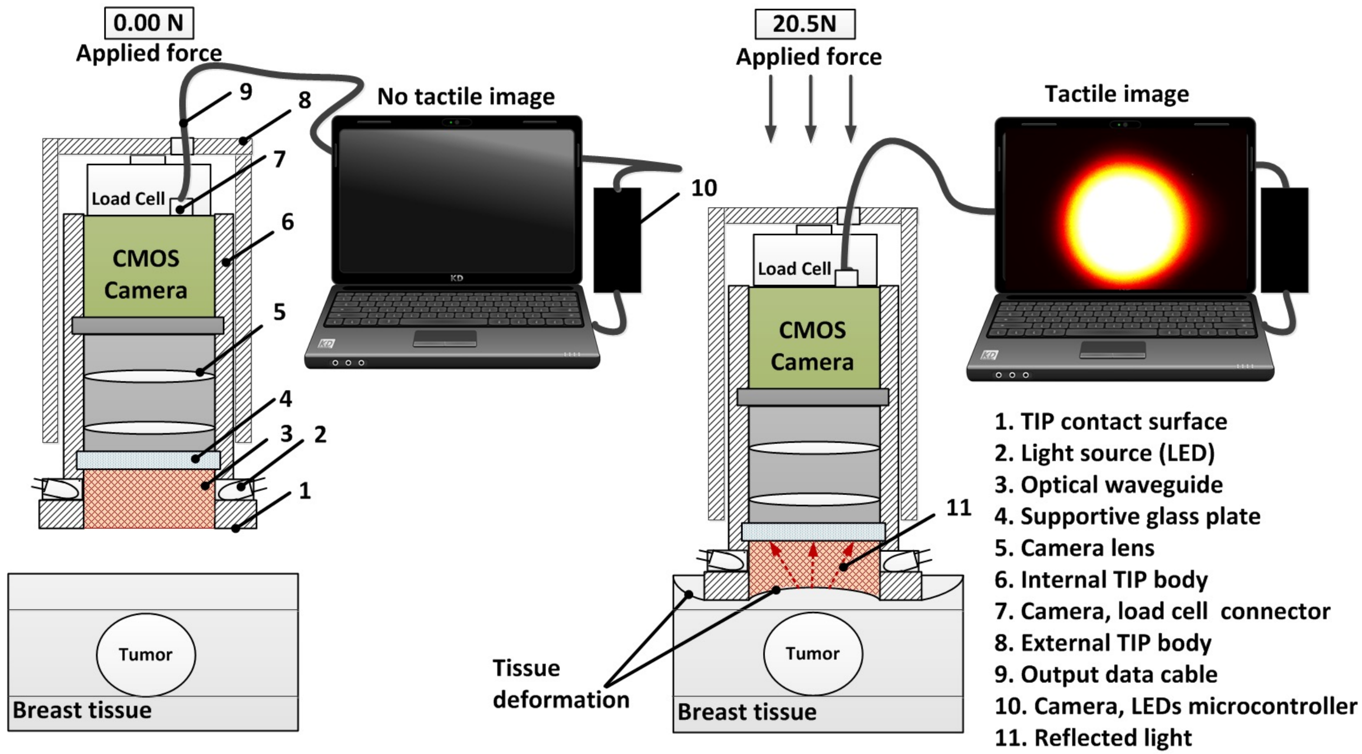
Tactile Imaging Probe's hardware and software are developed to measure tactile properties, such as the tumor size, stiffness, and depth within the breast tissue.

Multispectral Imaging Probe's hardware and software are developed to characterize superficial breast tissue properties, such as asymmetry, texture, and inflammation.

Finally, we developed the **Multimodal Index method** for individualized breast cancer risk assessment using two imaging modalities and the patient's health information.

Tactile Imaging Probe - Design

Malignant breast tumors tend to be stiffer and larger than benign tumors with tactile imaging modality,
we characterize tumors' size, stiffness, and depth



Tactile Imaging Probe – Tumor Stiffness

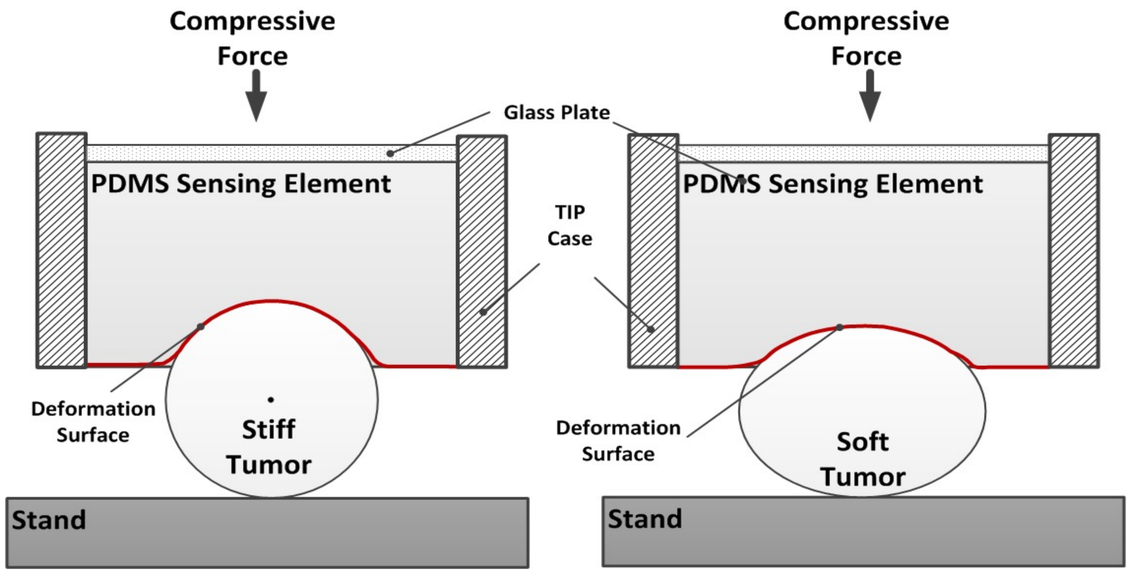


Figure : Stiff and soft tumors under TIP compression

Stiffness Estimation

Deformation force

$$\Delta f_i = f_i - f_{ref}$$

TIP sensing element deformation image

$$\Delta M = M_i - M_{ref}$$

Deformation Index of the imaged tumor

$$DI_i = \frac{\sum_{l=1}^{n} \sum_{k=1}^{m} \Delta M_i^{l,k}}{\Delta f_i}$$

TIP – Aquisition/Results

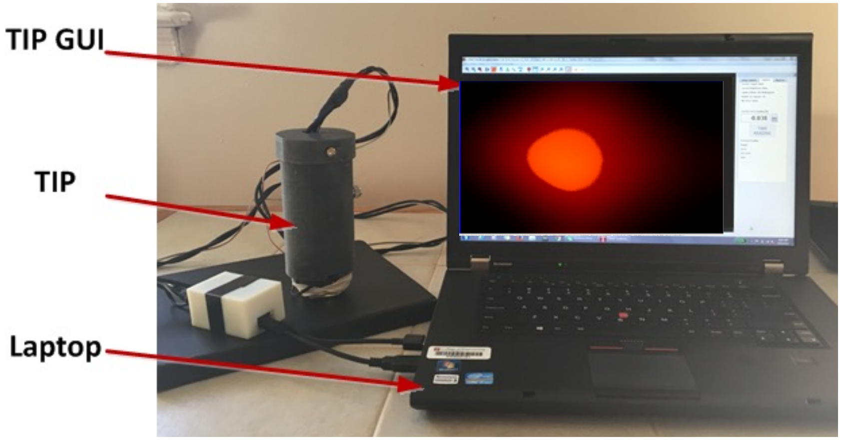


Figure : TIP connected to a laptop with TIP GUI

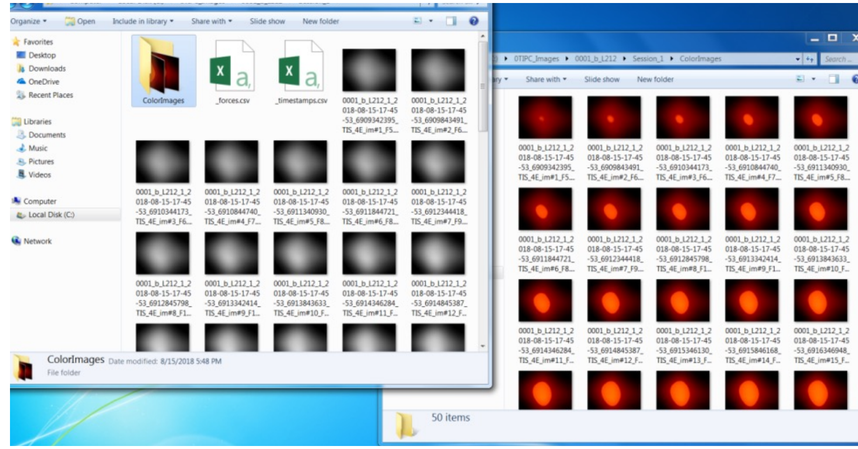


Figure : Acquired grayscale and colored tactile images

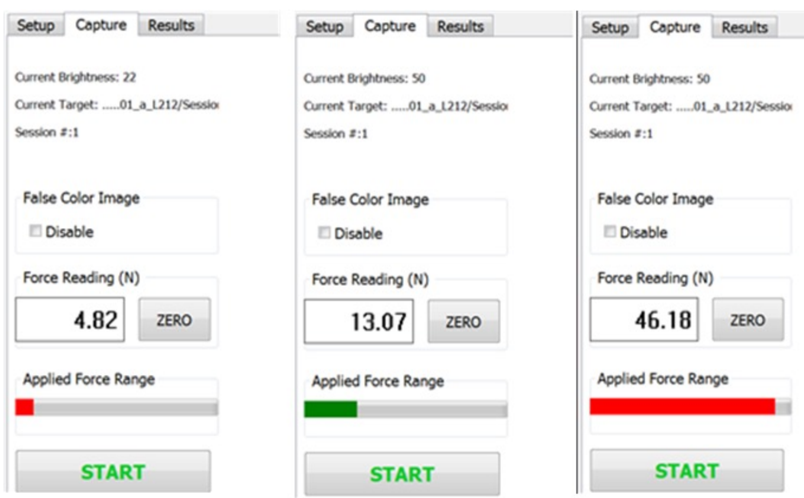


Figure : GUI capture view

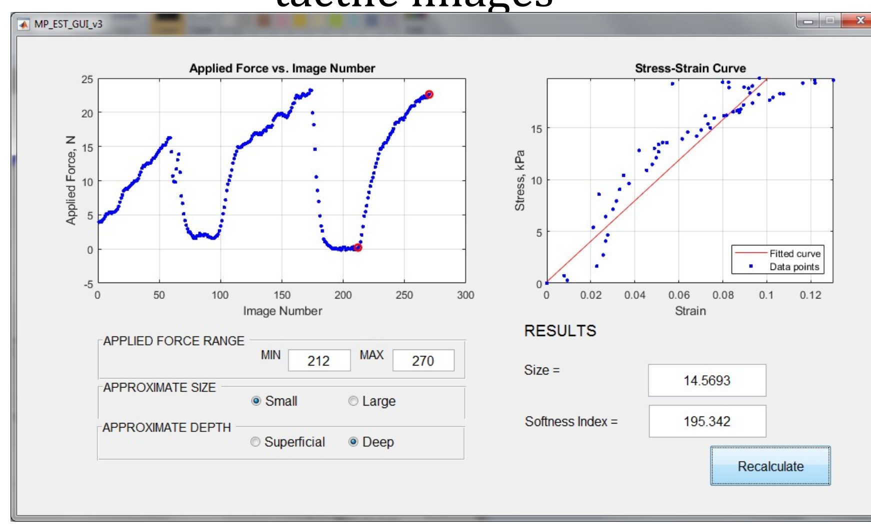
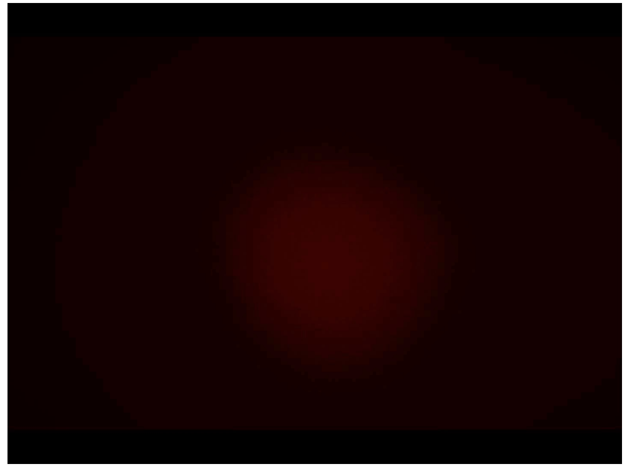
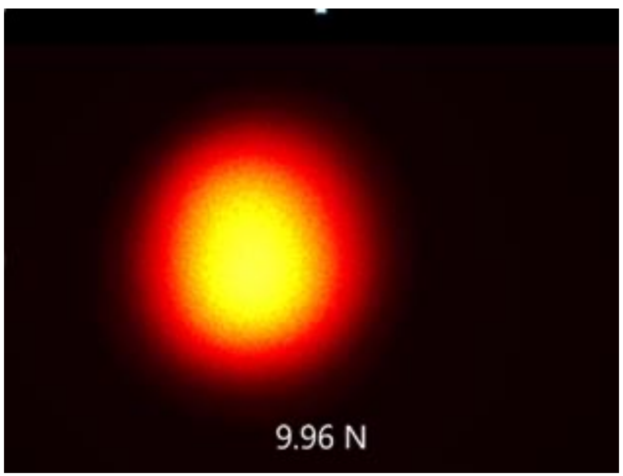


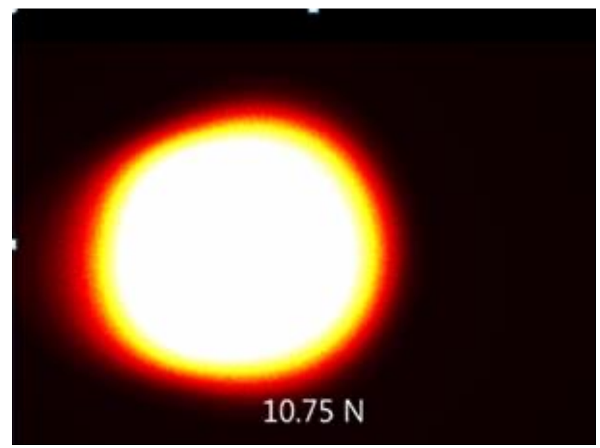
Figure : Result Calculation

Tactile Imaging Probe - Imaging





Soft Tumor   Size 15 mm



Stiff Tumor   Size 15 mm

Each lesion will have about 50 tactile images

Tactile Imaging Probe - TPD

Tactile Profile Diagram is a representative pattern image, which encodes differential tactile information from a set of TIP images.

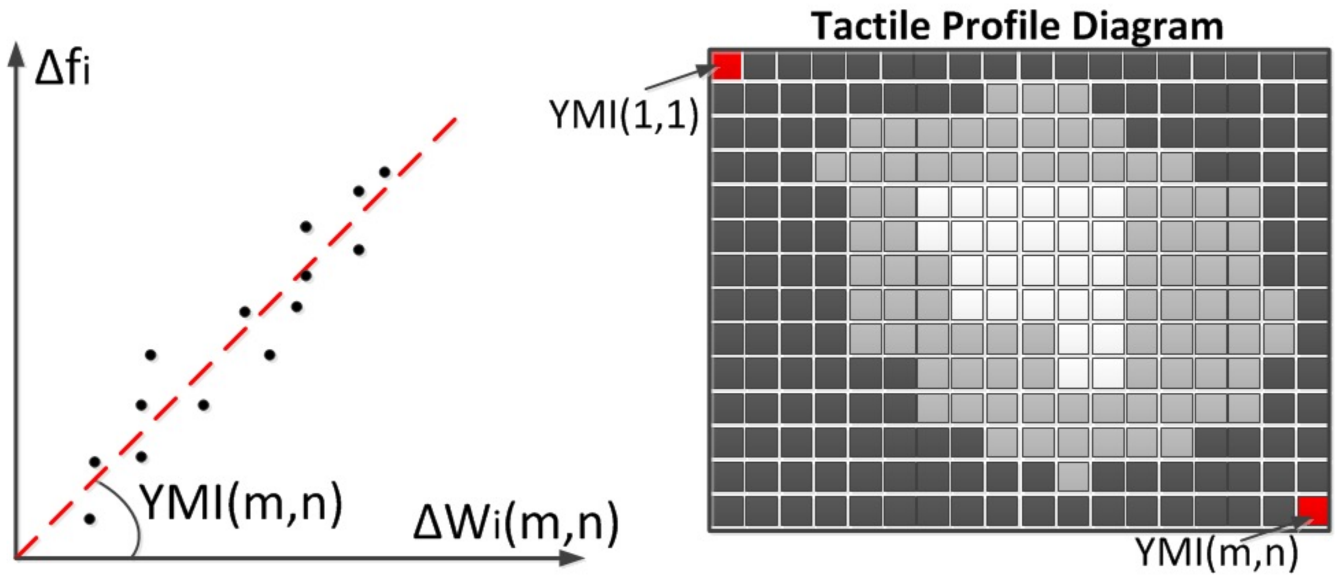


Figure : Construction of a Tactile Profile Diagram

Change in compression force $\Delta f_i = f_i - f_{ref}$

Reduced image $\Delta R_i(m,n) = R_i(m,n) - R_{ref}(m,n)$

Change of deformation image $\Delta W_i(m,n) = \Delta R_{max} - \Delta R_i(m,n)$

Tactile Imaging Probe - TPDs

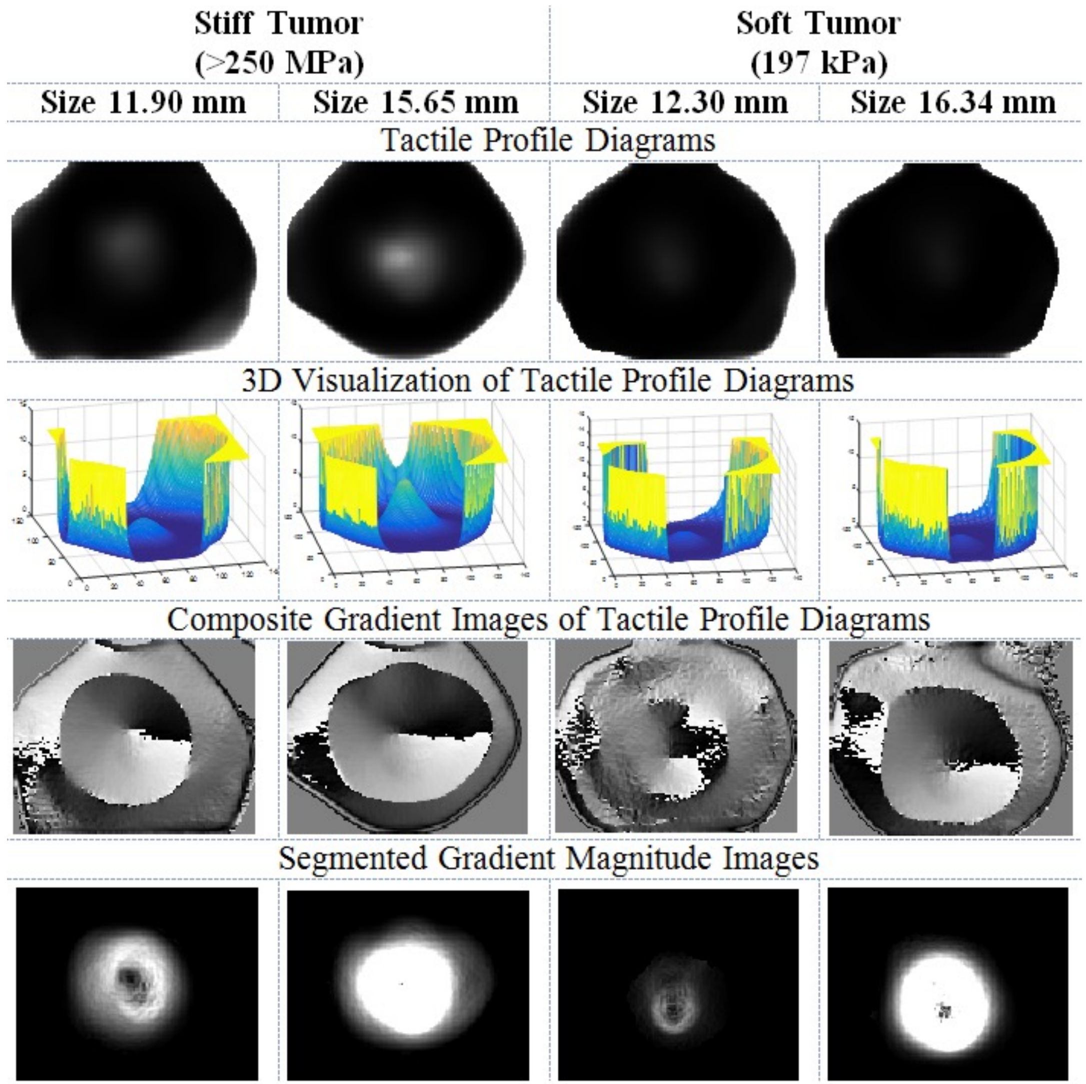


Figure : Examples of TPDs for the tumors with different size and stiffness

Tactile Imaging Probe – TPD Calculation

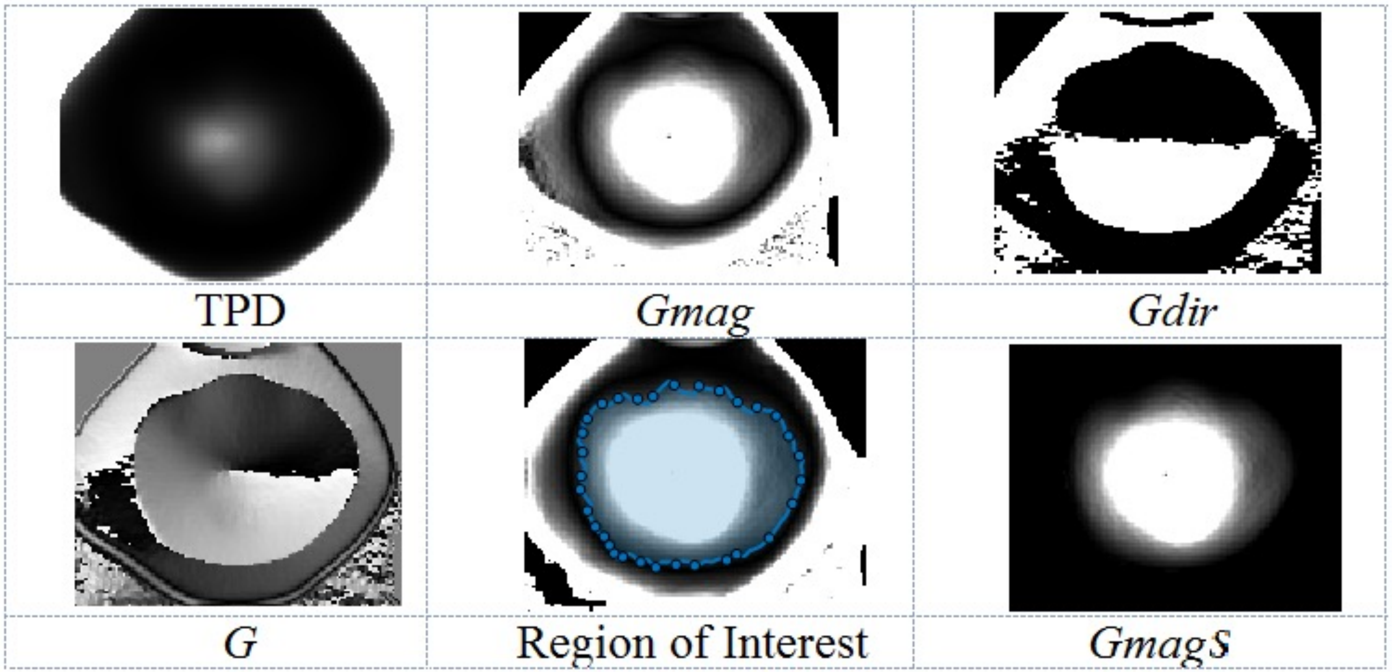


Figure : TPD segmentation for the tumor size and stiffness estimation

Size Estimation

$$D = aN_p + b$$

Stiffness Estimation

$$SI = \frac{\sum_m \sum_n G_{magS}(m,n)}{N_p}$$

Classification with CNN

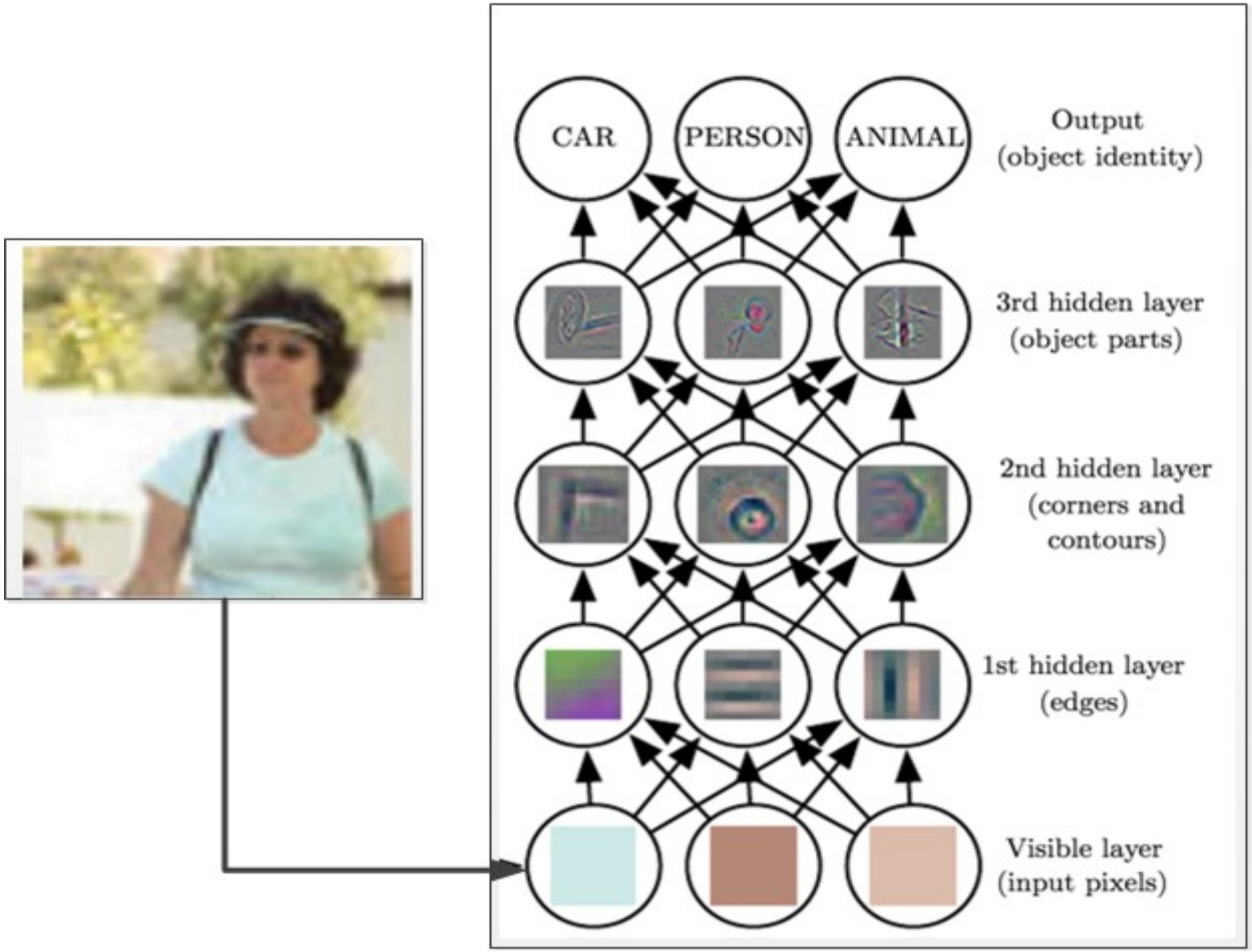
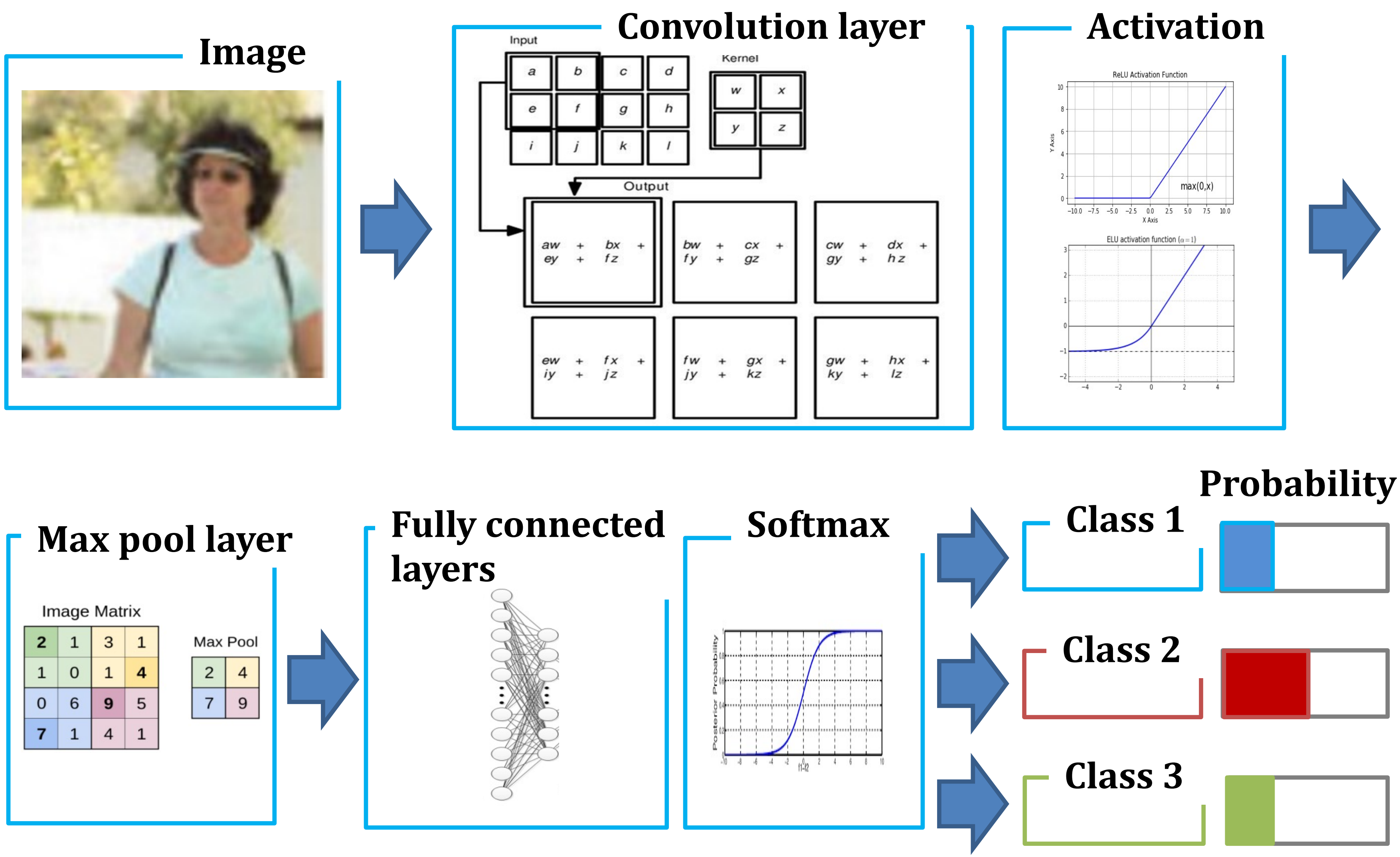


Figure : Image classification with CNN (Goodfellow, 2017)

Classification with CNN



Classification with CNN – TPD

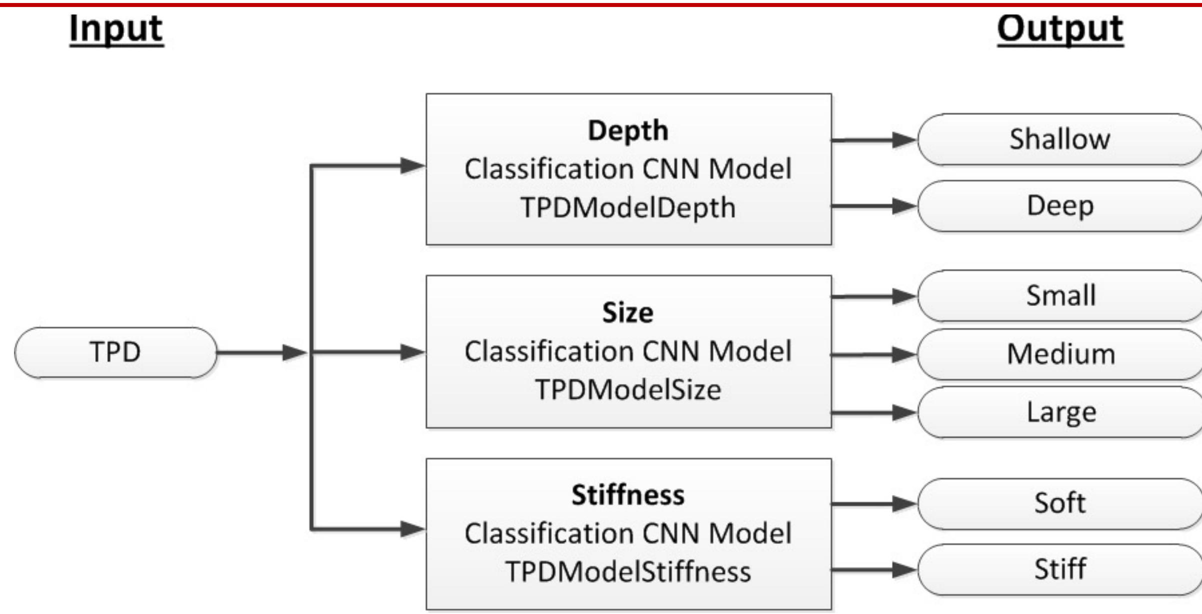


Figure : TPD classification diagram

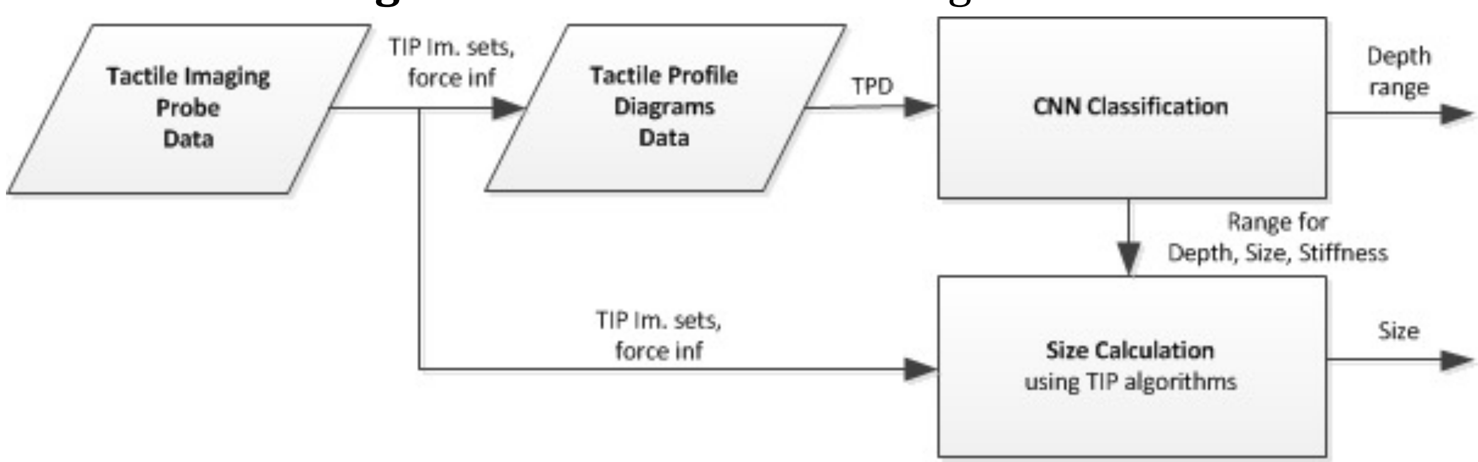


Figure : Accurate tumor size estimation

Classification with CNN – Stiffness (also depth, size)

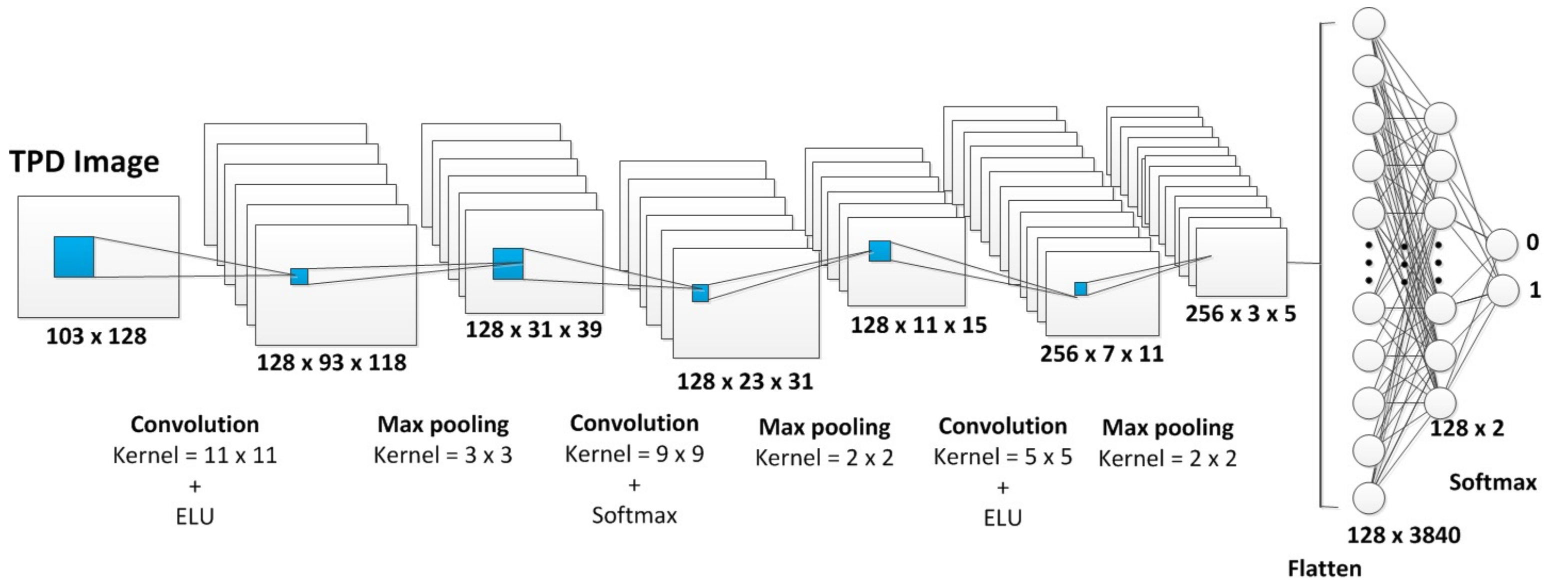


Figure : Stiffness CNN model (TPDModelStiffness)

Dataset

Sizes: 10 mm, 12 mm, 14 mm, 16 mm, 18 mm, 23 mm
Soft Subset: 130 kPa – 316 kPa
Stiff Subset: 376 kPa – 250 MPa
Depths: 0 mm, 2 mm, 4 mm, 6 mm, 8 mm, 10 mm
Data division: training 80% and validation 20%

Model trained on 6788 TPDs, validated on 1697 TPDs
Training: 50 epochs, 200 TPDs in a batch

Classification with CNN – Stiffness

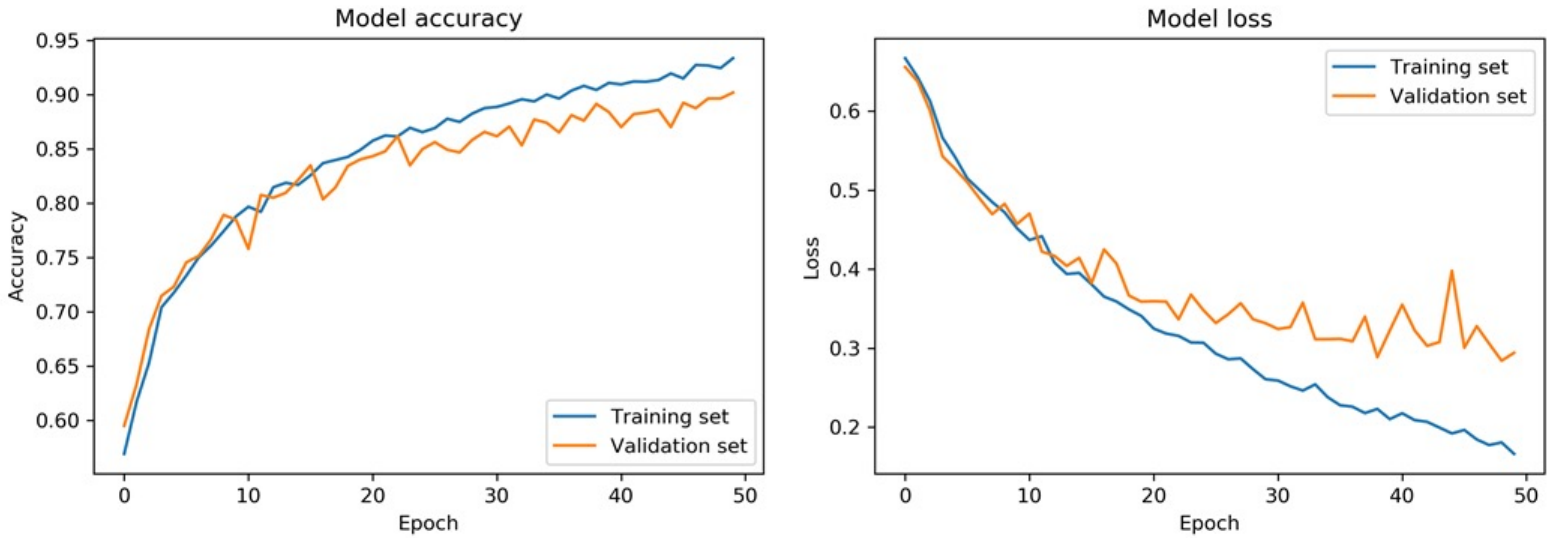


Figure : Graphs for TPDModelStiffness model accuracy and loss

Results

Validation accuracy = 0.90

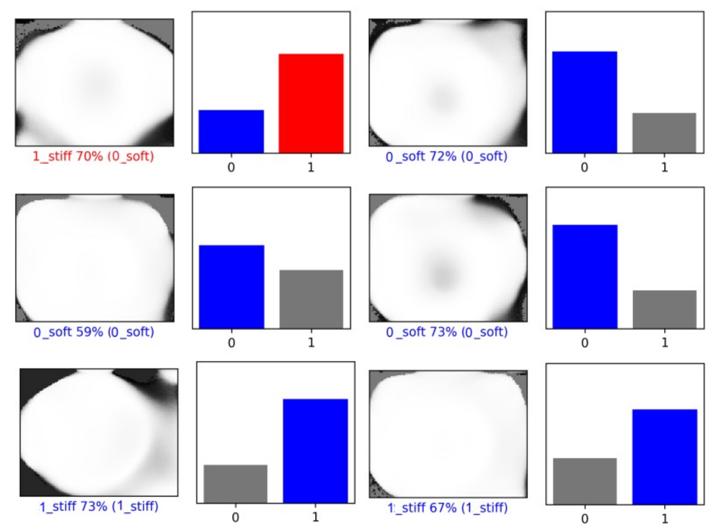


Figure : Examples of TPD classification with TPDModelStiffness

Classification with CNN – *in-Vivo* Results

Table : CNN classification results for the *in-vivo* data

Patient	Depth		Stiffness		Size	
	US Est. Class	CNN Class	Doctor Est. Class	CNN Class	US Est. Class	CNN Class
1	deep	shallow	soft	soft	small	small
2	shallow	shallow	stiff	stiff	small	small
3	shallow	shallow	stiff	stiff	small	large
4	shallow	shallow	soft	soft	medium	medium
5	shallow	shallow	stiff	stiff	medium	medium
6	shallow	shallow	soft	soft	medium	small
7	shallow	shallow	soft	soft	large	large
8	deep	deep	soft	soft	large	large
9	shallow	shallow	soft	soft	large	medium
10	deep	deep	soft	stiff	large	large
11	shallow	shallow	stiff	stiff	large	large
12	shallow	shallow	stiff	stiff	large	small
13	shallow	shallow	stiff	stiff	large	large
Accuracy		0.92		0.92		0.69

Multispectral Imaging Probe

Even without a palpable tumor, there is a possibility of aggressive breast cancer such as IBC, which manifests by a rapidly developing inflammation.

With multispectral imaging modality, we characterize IBC manifestations, such as asymmetry, texture, and inflammation.

Multispectral Imaging Probe

- Biological tissues have **non-homogeneous** optical properties
- Light **scatters** and gets **absorbed** within tissue

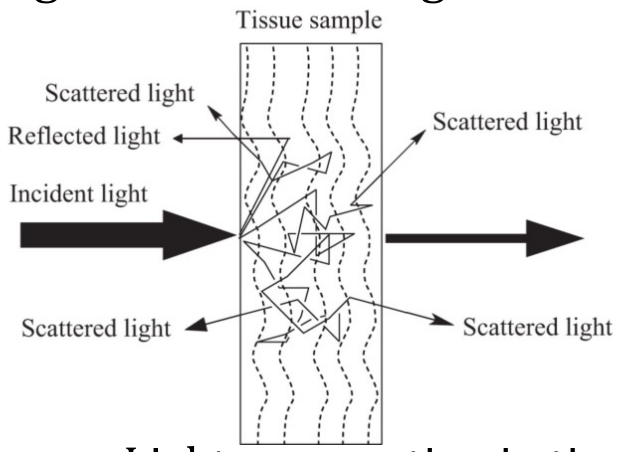


Figure : Light propagation in tissue

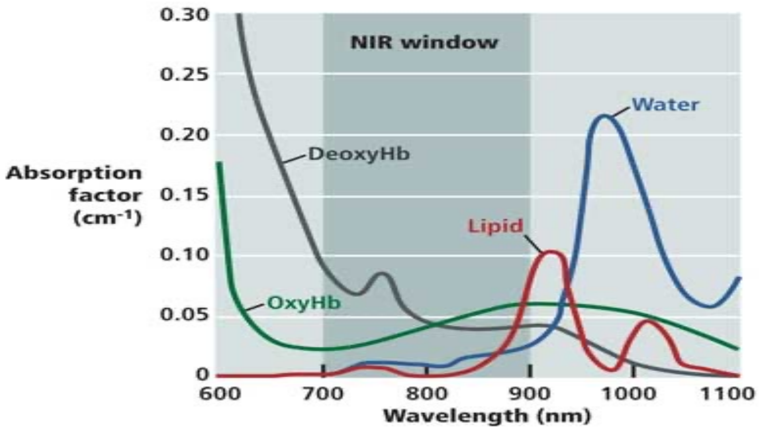


Figure : Absorption of tissue chromophores

- Hyperspectral/Multispectral Imaging can help characterize tissues

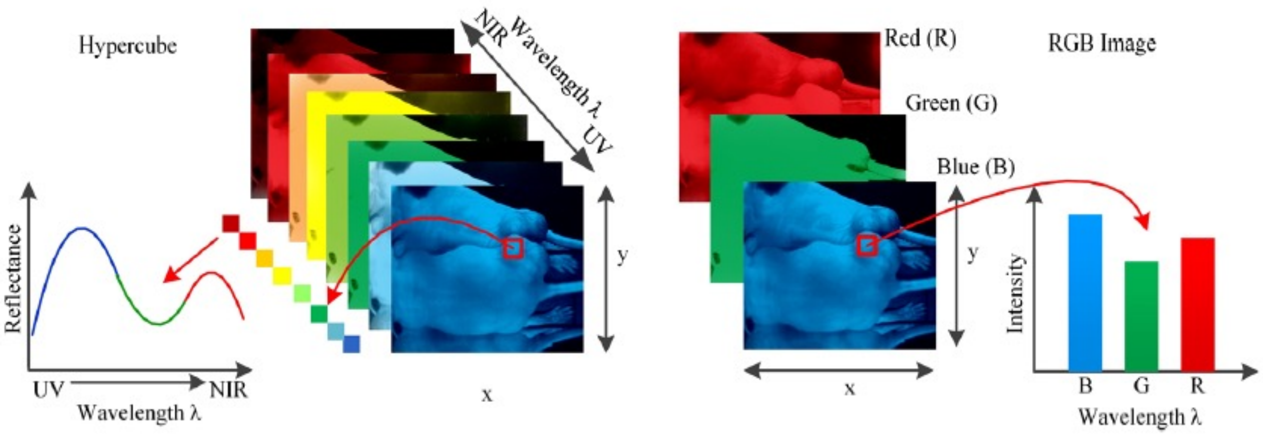


Figure : Hypercube image vs. RGB image

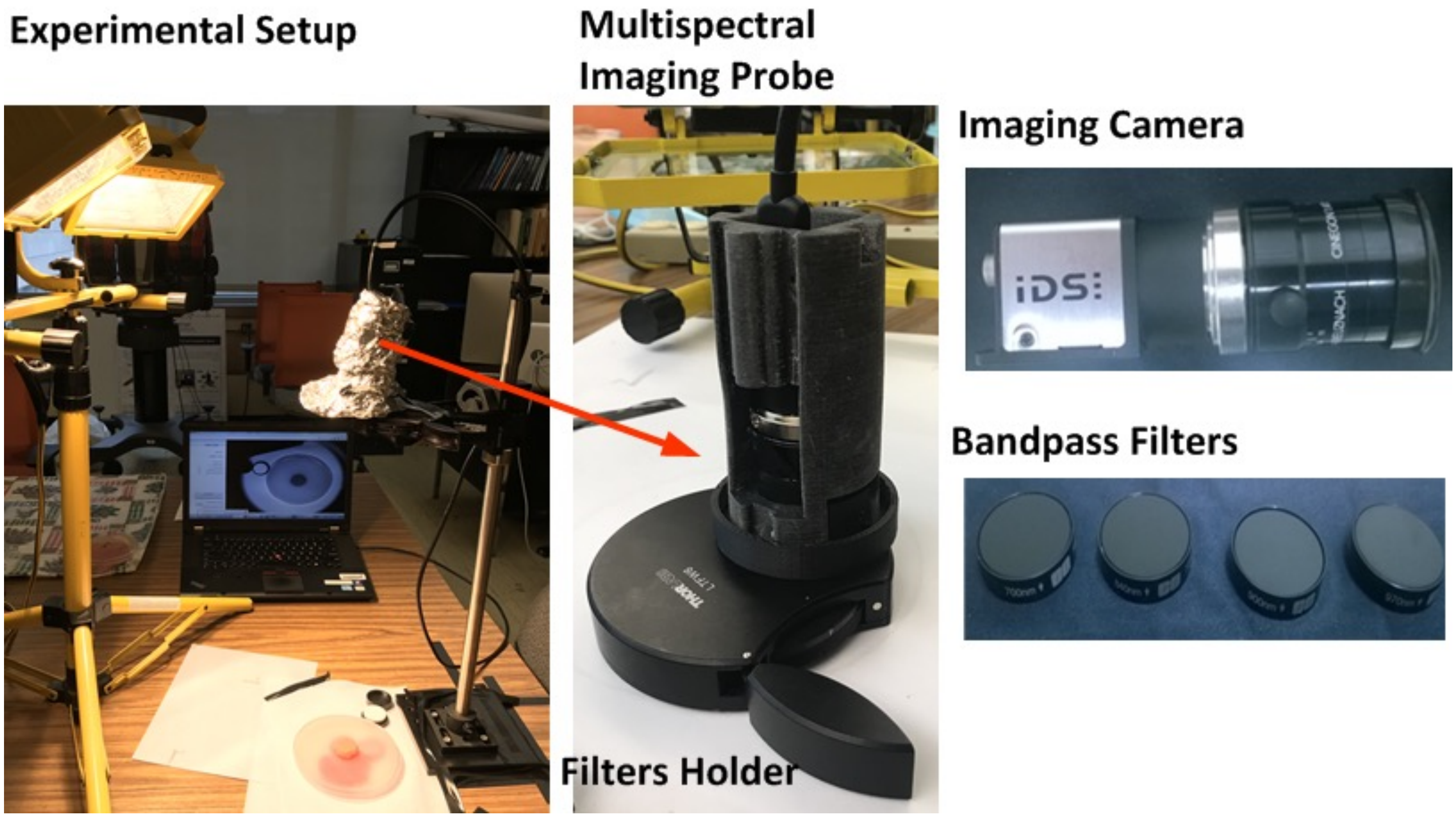


Figure : Multispectral Imaging Probe components and experimental setup

Multispectral Imaging Probe – Image Processing

Multispectral Image Pre-processing

Normalization

Decreases the effect of inhomogeneous illumination and hardware-related noise

$$I_{norm} = \frac{I_{raw} - I_{dark}}{I_{white} - I_{dark}}$$

Registration

Searches for geometric transformation of multiple images of the same scene to align

Construction of Multispectral Profile Diagram

Carries unique information about the optical properties of breast tissue from four imaging bands consolidated in one pattern image.

Construction of Differential Multispectral Profile Diagram

Carries unique information about the breast tissue changes.

Multispectral Imaging Probe - MPD

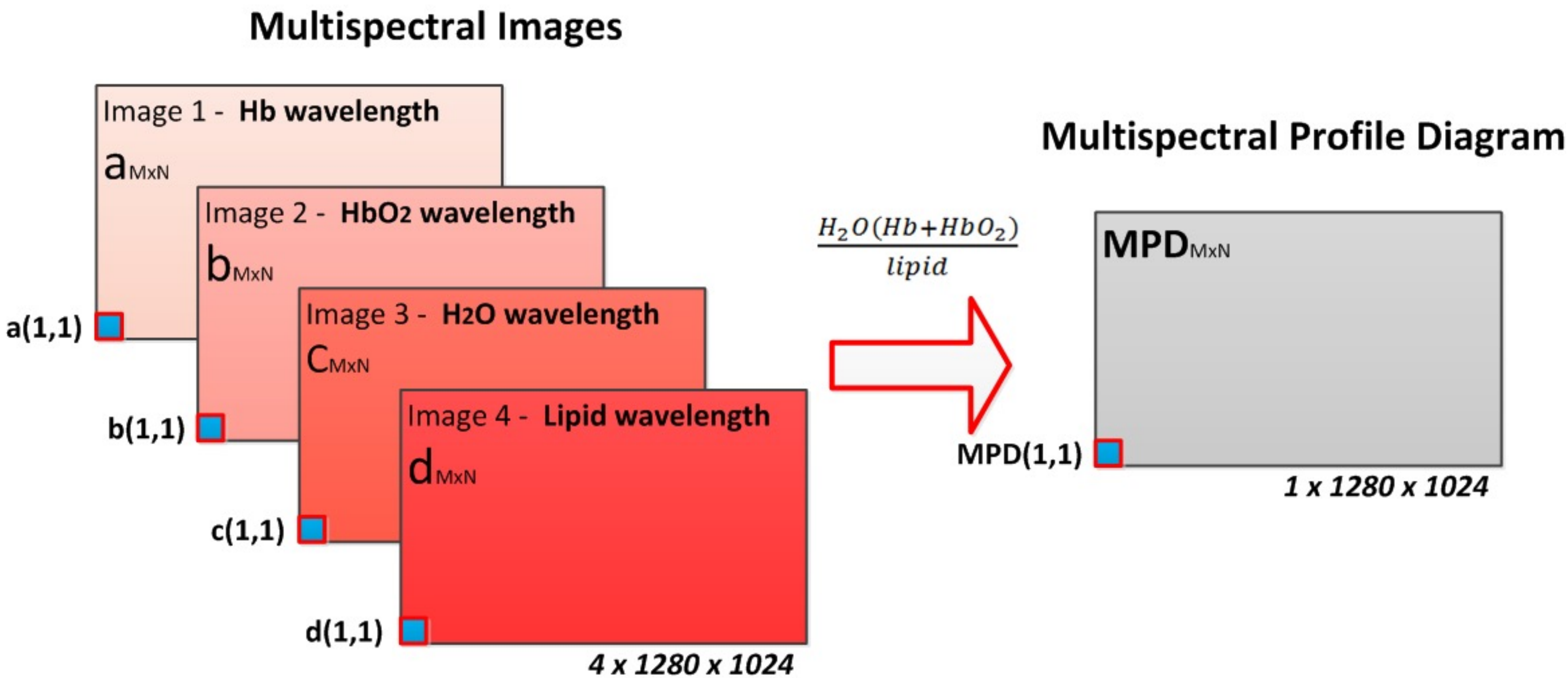


Figure : Construction of Multispectral Profile Diagram

$$MPD_{M\times N} = \begin{bmatrix} \frac{c_{1,1}(a_{1,1}+b_{1,1})}{d_{1,1}}, & \frac{c_{1,2}(a_{1,2}+b_{1,2})}{d_{1,2}}, & \cdots & \frac{c_{1,N}(a_{1,N}+b_{1,N})}{d_{1,N}} \\ \frac{c_{2,1}(a_{2,1}+b_{2,1})}{d_{2,1}}, & \frac{c_{2,2}(a_{2,2}+b_{2,2})}{d_{2,2}}, & \cdots & \frac{c_{2,N}(a_{2,N}+b_{2,N})}{d_{2,N}} \\ \vdots & \vdots & \ddots & \vdots \\ \frac{c_{M,1}(a_{M,1}+b_{M,1})}{d_{M,1}}, & \frac{c_{M,2}(a_{M,2}+b_{M,2})}{d_{M,2}}, & \cdots & \frac{c_{M,N}(a_{M,N}+b_{M,N})}{d_{M,N}} \end{bmatrix}$$

Multispectral Imaging Probe - Phantom

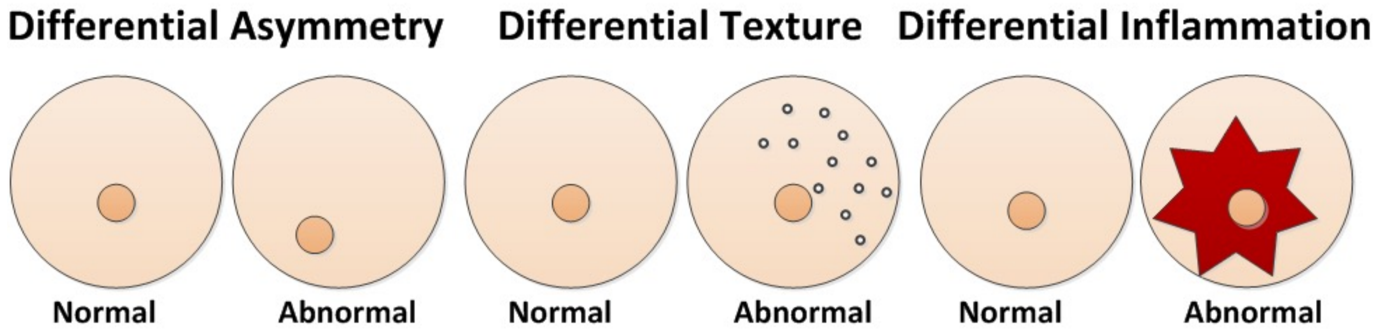


Figure : MIP Phantom design

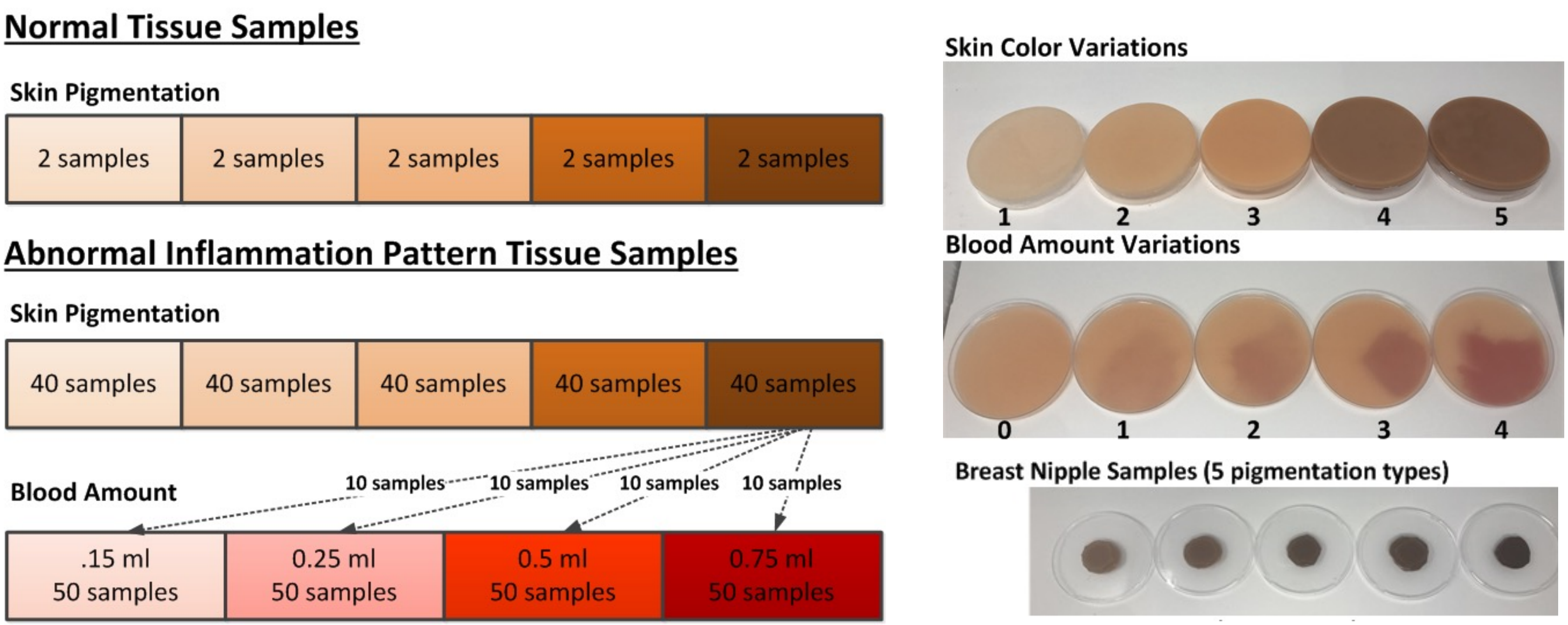


Figure : MIP Phantom implementation

MIP – Multispectral Profile Diagram

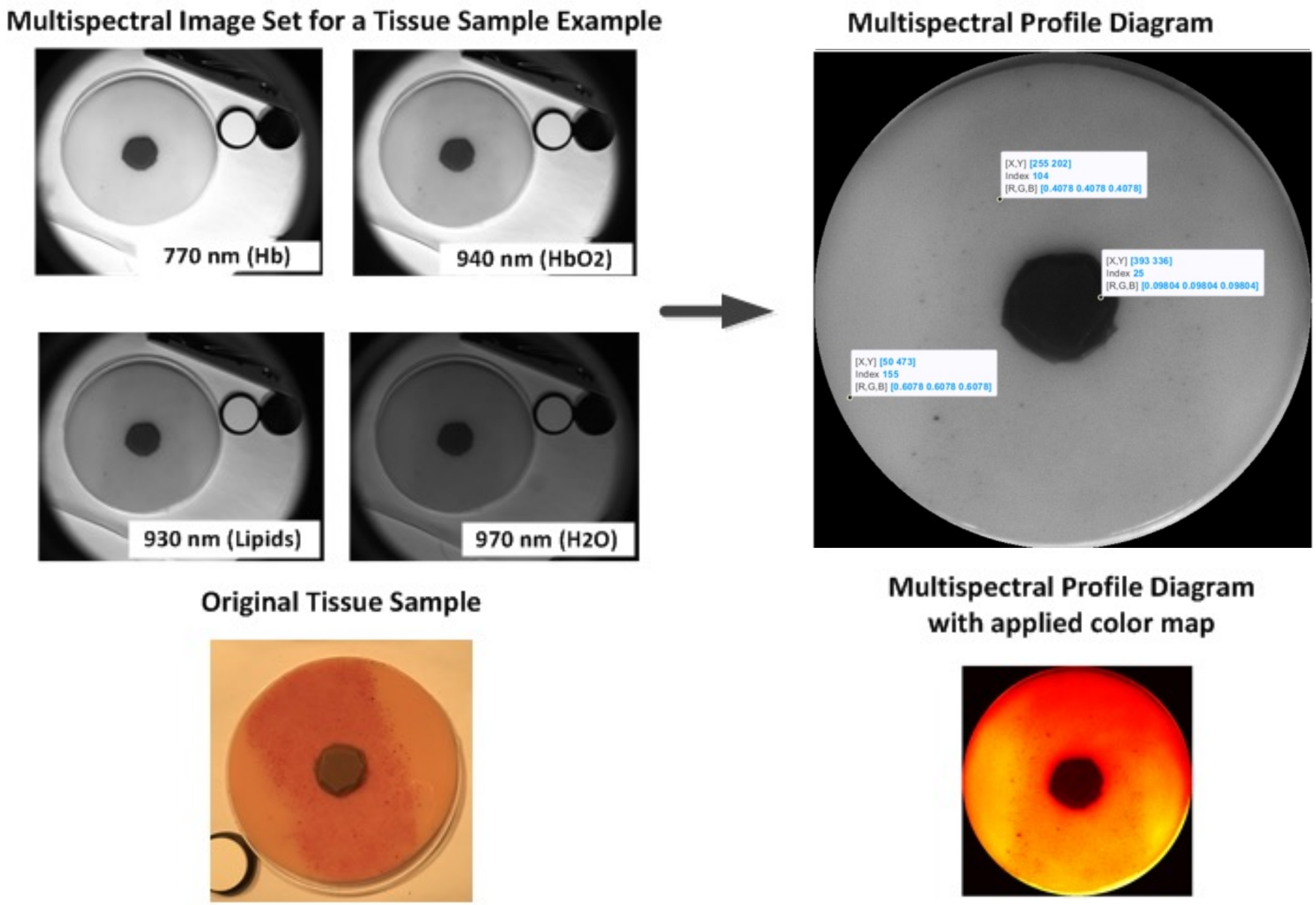


Figure : Construction of Multispectral Profile Diagram

MIP – Enhanced Differential MPD

$$MPD_{diff} = \left| K \times MPD_{Abnormal} - MPD_{SNormal} \right|,$$

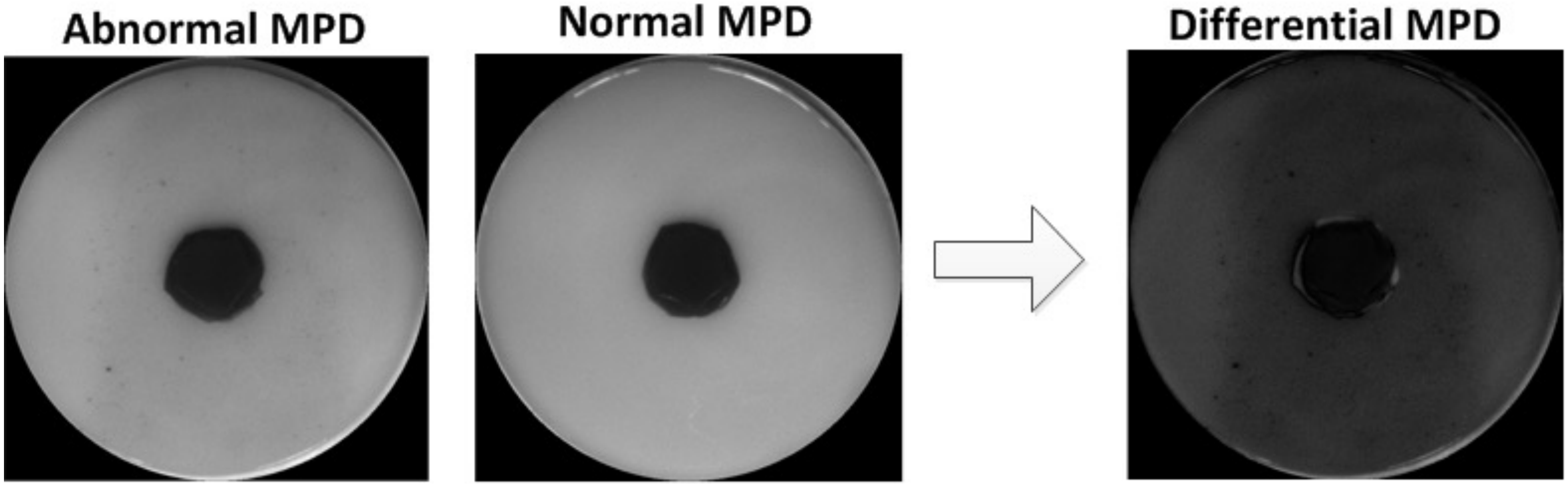


Figure : Differential Multispectral Profile Diagram construction

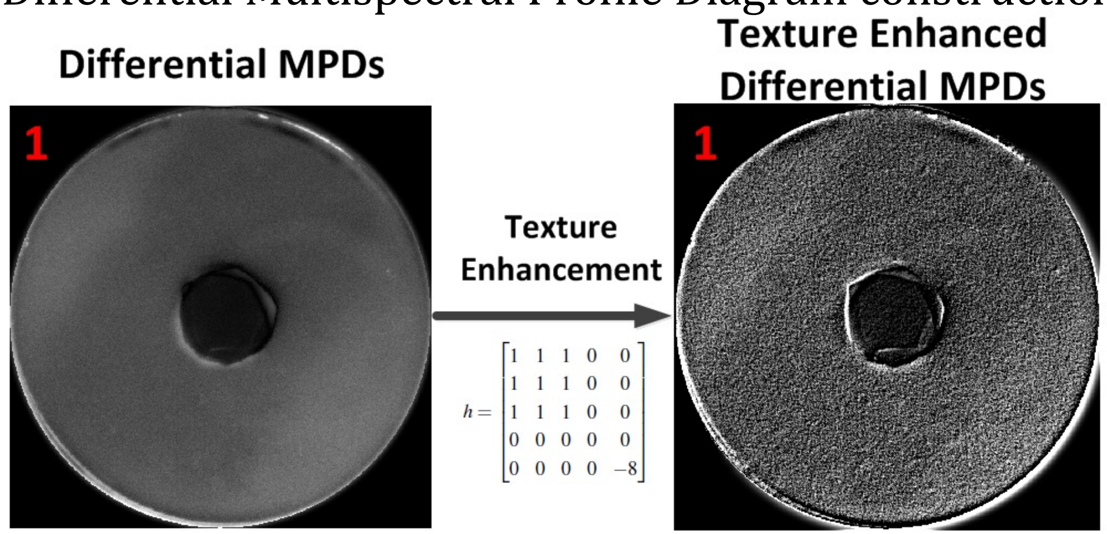


Figure : Texture enhancement using Differential Multispectral Profile Diagram

Classification with CNN - MPD

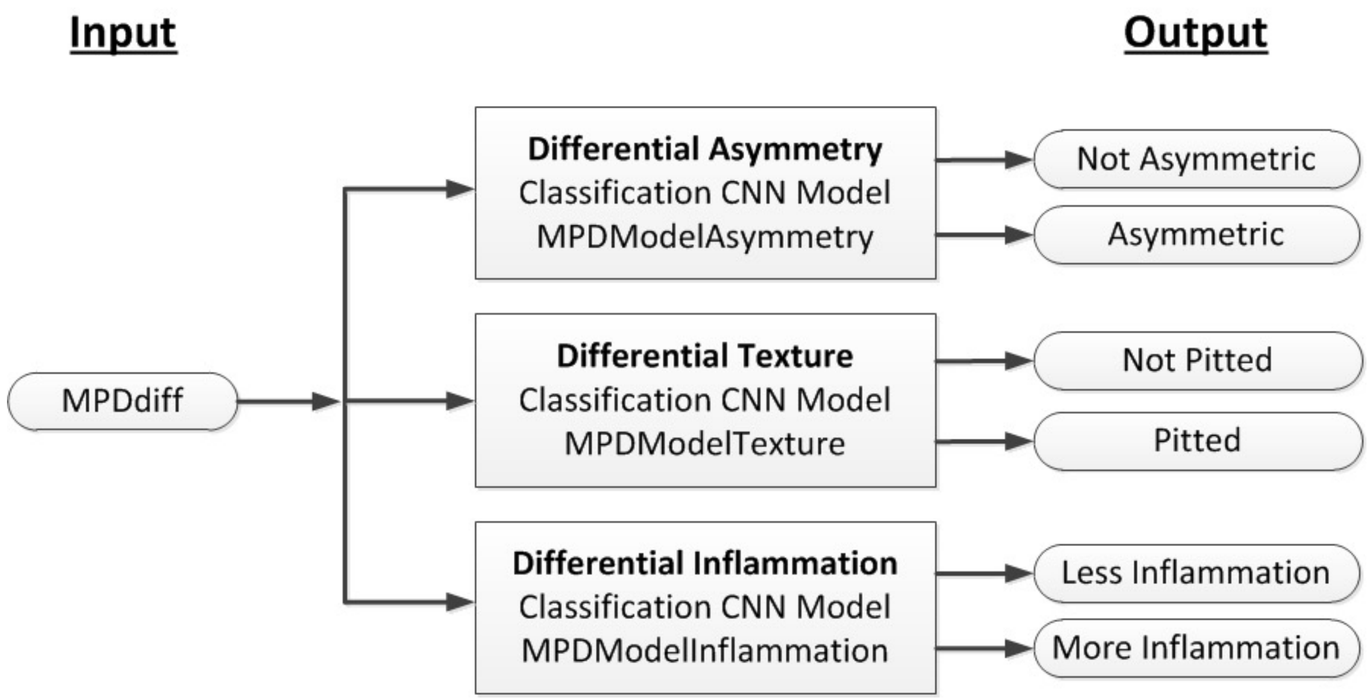


Figure : Multispectral Profile Diagram classification with CNN

Classification with CNN - Datasets

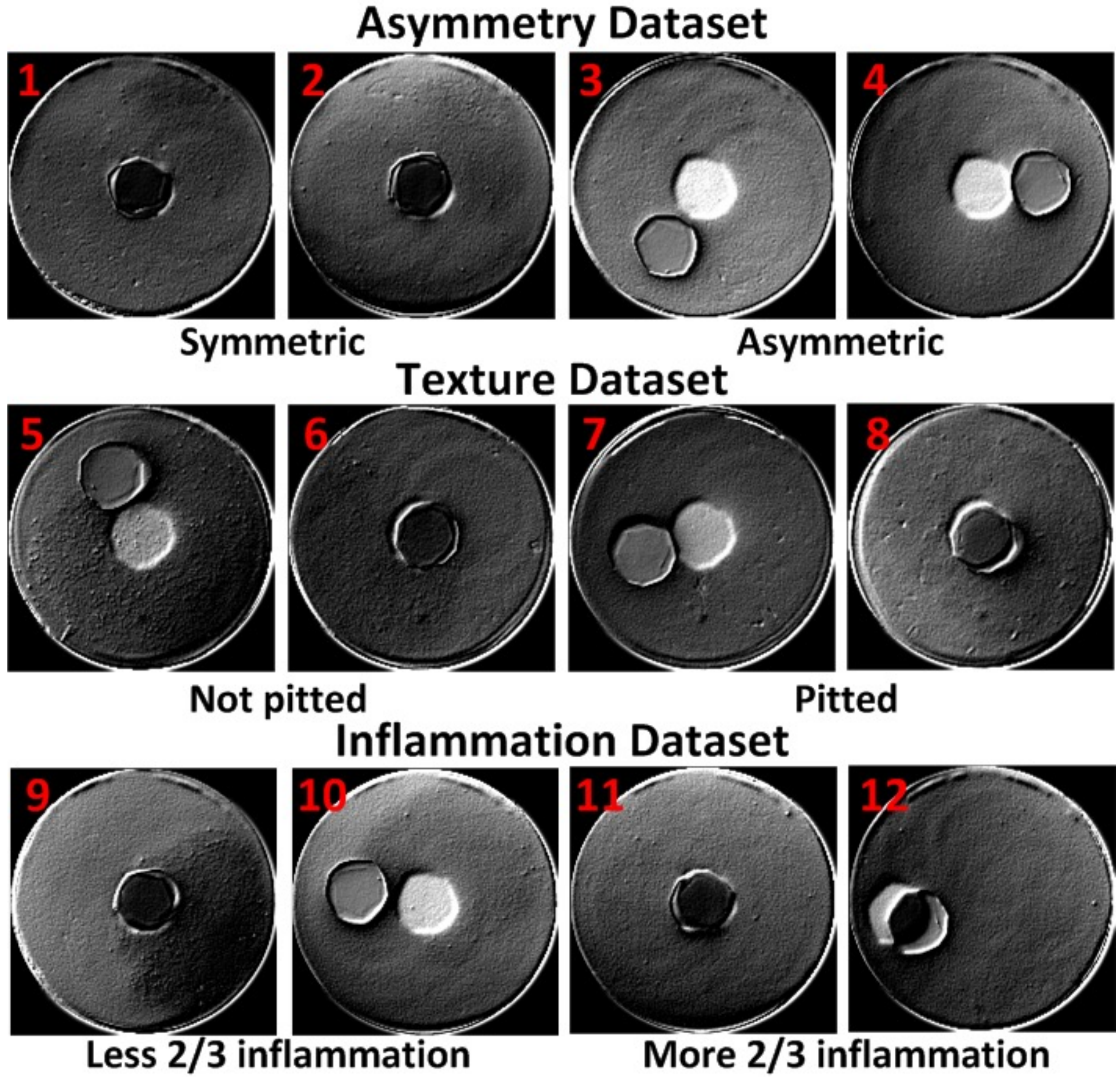


Figure : Examples of Differential Multispectral Profile Diagrams Datasets

Classification with CNN – Asymmetry (also texture, inflammation)

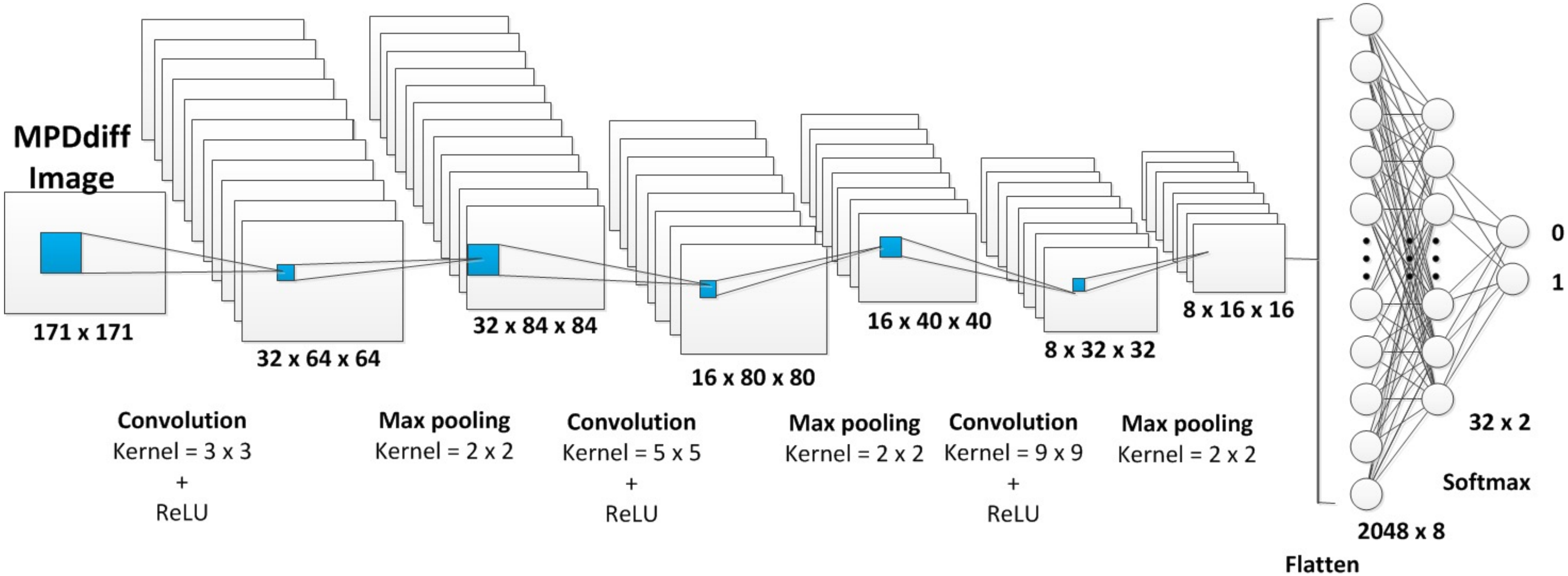


Figure : Asymmetry CNN Model (MPDModelAsymmetry)

Dataset

The samples were obtained from pairwise combinations of 240 affected and 6 normal MPDs of MIP samples with different combinations of phantom features.
Data division: Training 75%, validation 20%, and test 5%.

Model trained on 30720 MPDs
validated on 7656 MPDs
tested on 1344 MPDs
Training: 5 epochs, 100 MPDs in a batch

Classification with CNN – Asymmetry (also texture, inflammation)

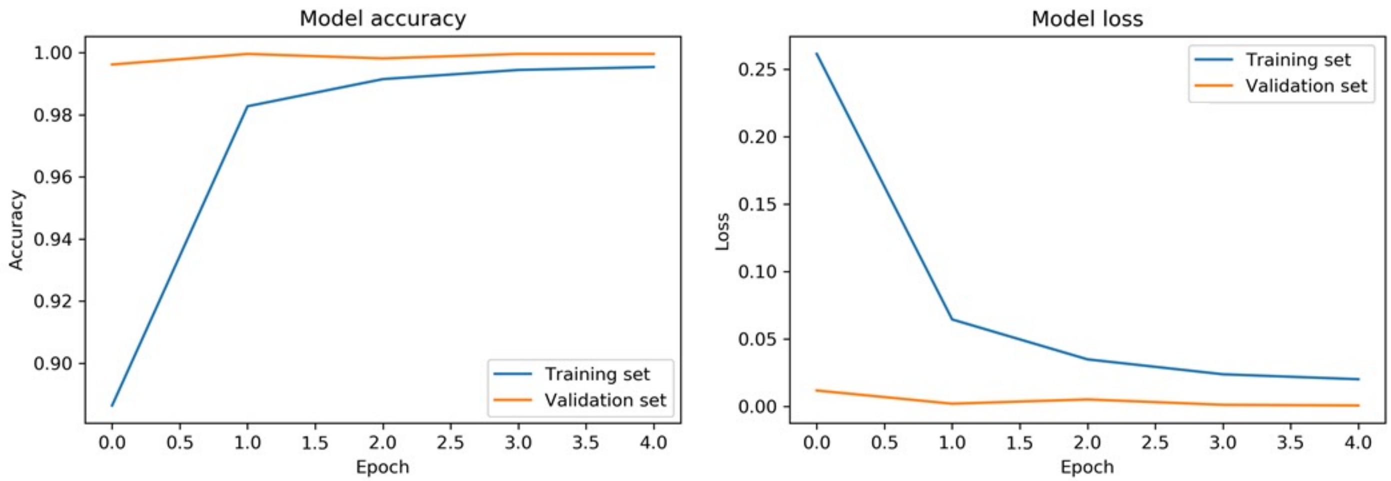


Figure : Graphs for MPDModelAsymmetry model accuracy and loss

Results

training accuracy, 99%,
validation accuracy, 100%
test accuracy, 98%

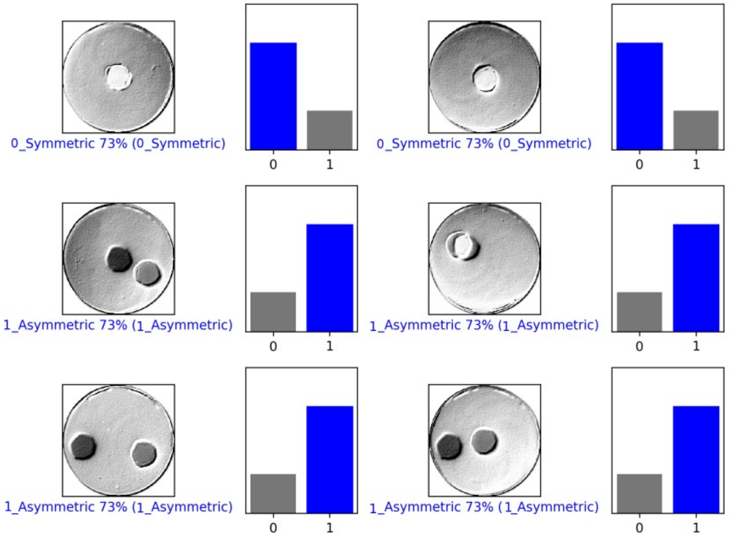


Figure : Examples of TPD classification with MPDModelAsymmetry

Classification with CNN – Phantom Test Set

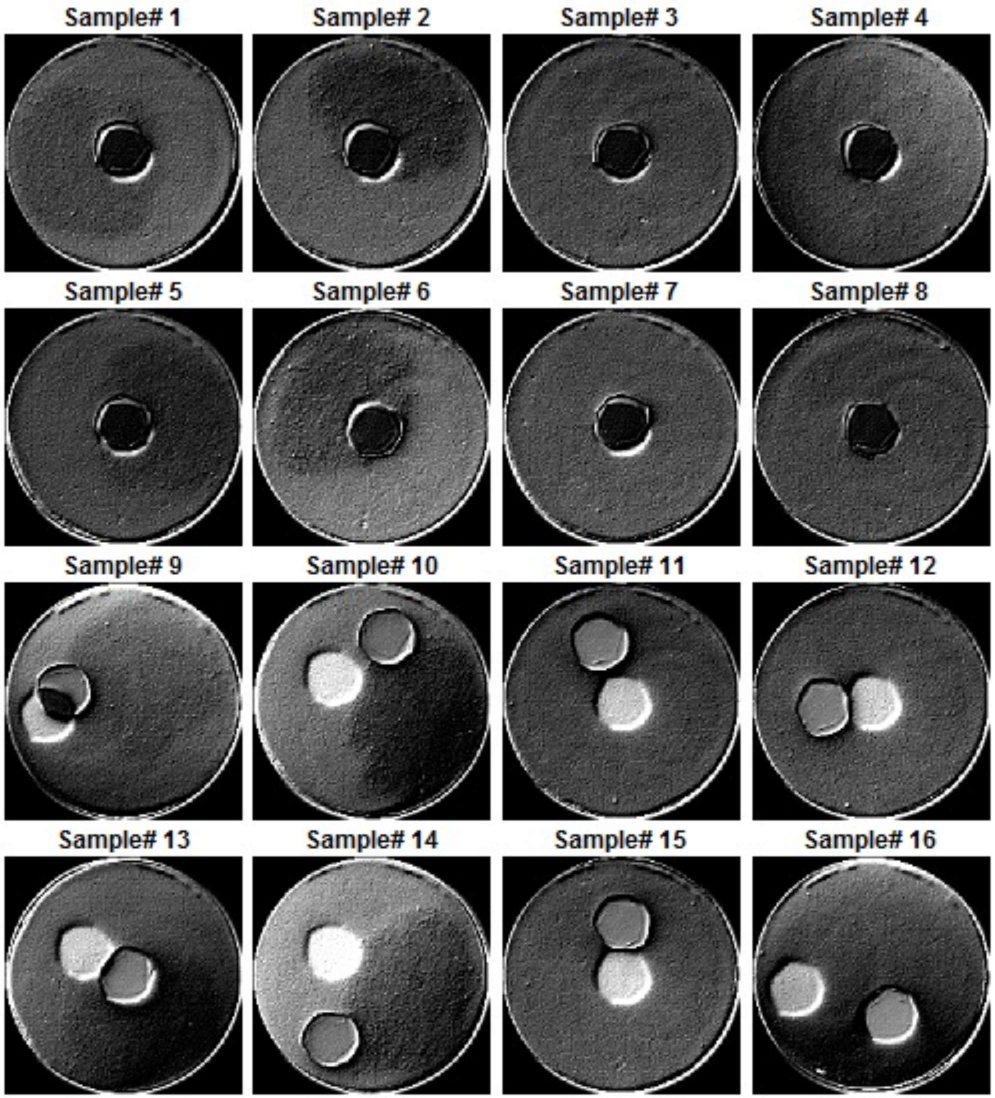


Figure : Independent classification test samples

Figure : Independent test samples

Sample	Blood Amount, ml	Inflammation Area, %	Added Features
1	0.50	40	-
2	0.75	40	-
3	0.50	95	-
4	0.75	95	-
5	0.50	40	Pitted
6	0.75	40	Pitted
7	0.50	95	Pitted
8	0.75	95	Pitted
9	0.50	40	Asymmetric
10	0.75	40	Asymmetric
11	0.50	95	Asymmetric
12	0.75	95	Asymmetric
13	0.50	40	Asym Pitted
14	0.75	40	Asym Pitted
15	0.50	95	Asym Pitted
16	0.75	95	Asym Pitted

Classification with CNN - Results

Table : MPD classification results on an independent dataset

Sample	Asymmetry CNN Class Prob.		Texture CNN Class Prob.		Inflammation CNN Class Prob.	
	Sym.	Asym.	NotPit.	Pitted	Small Infl.	Large Infl.
1	1.00	0.00	1.00	0.00	0.96	0.04
2	1.00	0.00	1.00	0.00	0.99	0.01
3	1.00	0.00	1.00	0.00	0.96	0.04
4	1.00	0.00	1.00	0.00	0.02	0.98
5	1.00	0.00	0.01	0.99	0.99	0.01
6	1.00	0.00	0.00	1.00	1.00	0.00
7	1.00	0.00	0.12	0.88	0.23	0.77
8	1.00	0.00	0.00	1.00	0.36	0.64
9	0.00	1.00	1.00	0.00	0.76	0.24
10	0.00	1.00	1.00	0.00	1.00	0.00
11	0.00	1.00	1.00	0.00	0.01	0.99
12	0.00	1.00	0.99	0.01	0.03	0.97
13	0.00	1.00	0.01	0.99	0.97	0.03
14	0.00	1.00	0.05	0.95	1.00	0.00
15	0.00	1.00	0.14	0.86	0.00	1.00
16	0.00	1.00	0.99	0.01	0.69	0.31
Accuracy		1.00		0.94		0.88

Note: The gray color indicates true Asymmetry class samples, the green color shows the true Pitted class samples, and the pink color highlights the true Large Inflammation class samples. Misclassified samples are indicated with red font color.

Multimodal Index

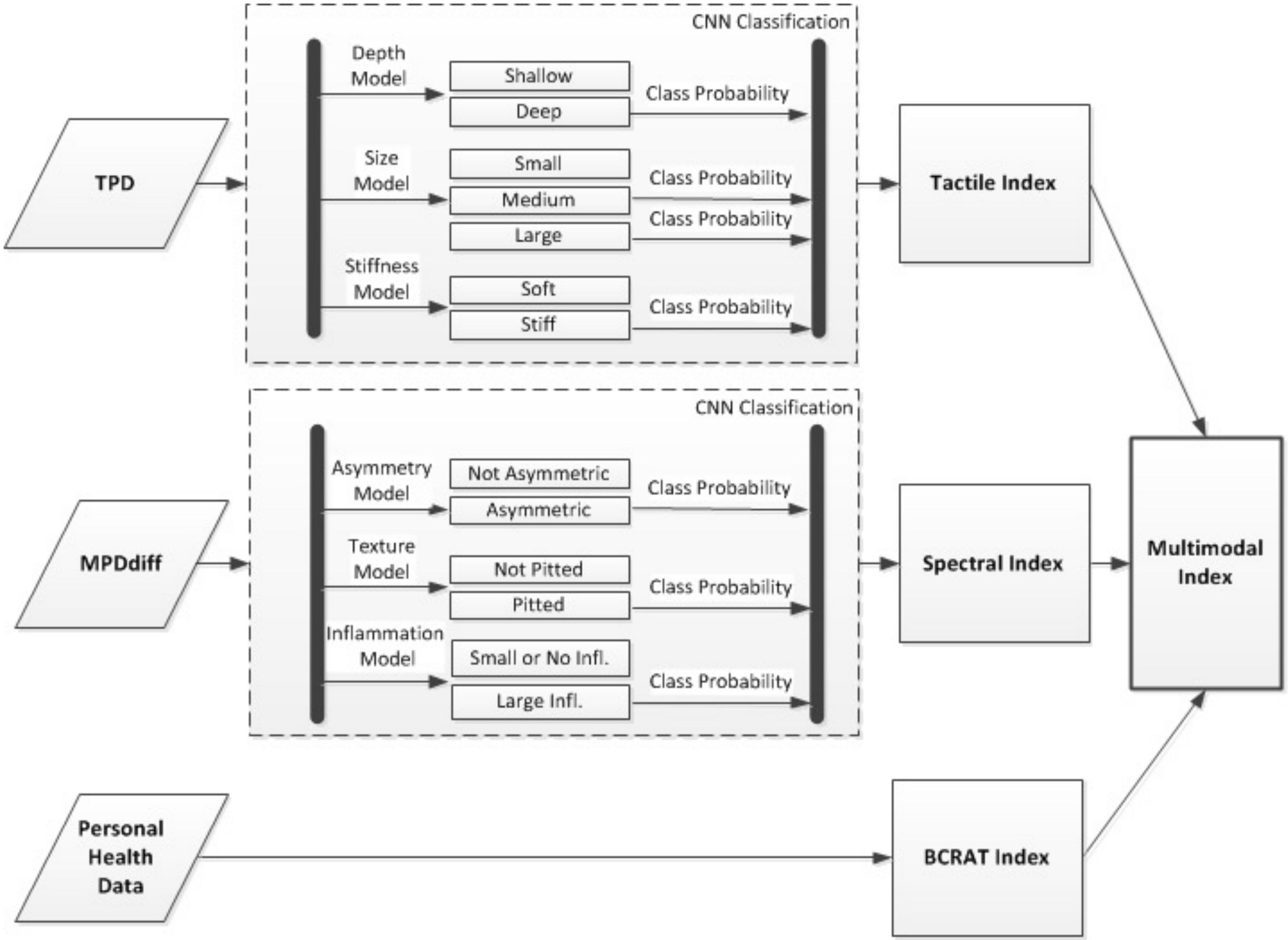


Figure : Block diagram for Multimodal Index computation

Multimodal Index – BCRAT Index

- The BCRAT Index is the individual risk of developing breast cancer established by NCI based on Gail statistical model
- The online BCRAT calculation tool is publicly available.

1. Does the woman have a medical history of any breast cancer or of ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS) or has she received previous radiation therapy to the chest for treatment of Hodgkin lymphoma?
2. Does the woman have a mutation in either the *BRCA1* or *BRCA2* gene, or a diagnosis of a genetic syndrome that may be associated with elevated risk of breast cancer?
3. What is the patient's age?
4. What is the patient's race/ethnicity?
   a. What is the sub race/ethnicity or place of birth?
5. Has the woman ever had a breast biopsy?
   a. How many breast biopsies (positive or negative) has the woman had?
   b. Has the woman ever had a breast biopsy with atypical hyperplasia?
6. What was the woman's age at the time of her first menstrual period?
7. What was the woman's age when she gave birth to her first child?
8. How many of the woman's first-degree relatives (mother, sisters, daughters) have had breast cancer?

Figure : The BCRAT calculator questions

5–Year Risk of Developing Breast Cancer	
Patient Risk	Average Risk
0.4%	**0.3%**

Lifetime Risk of Developing Breast Cancer	
Patient Risk	Average Risk
10.4%	**12.6%**

Figure : Example of the NCI BCRAT calculator results

Multimodal Index

Tactile Index

$$Index_T = \alpha_1 P_{11} + \alpha_2 P_{12} + \alpha_3 P_{13},$$

Spectral Index

$$Index_S = \beta_1 P_{21} + \beta_2 P_{22} + \beta_3 P_{23},$$

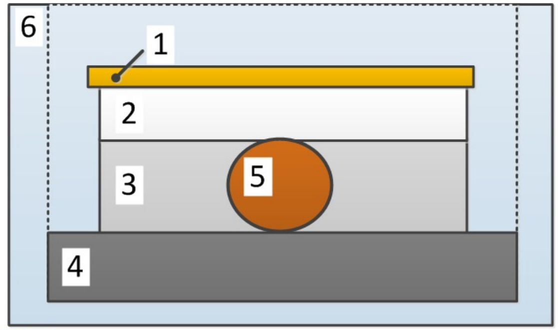
BCRAT Index

$$Index_{BCRAT} = P_{31},$$

Multimodal Index

$$Multimodal\ Index = w_1 Index_T + w_2 Index_S + w_3 Index_{BCRAT},$$

Multimodal Index – Phantom



1. Multispectral layer	PDMS 1:2 Ratio + absorption and scattering agents	94 kPa
2. Depth layer	PDMS 1:2 Ratio	94 kPa
3. Intermediate layer	PDMS 1:2 Ratio	94 kPa
4. Base layer	PDMS 1:20 Ratio	629 kPa
5. Tumor Phantom	PDMS Ratios	130 kPa ... 629 kPa
6. Pyrex glass container		

Figure : Bimodal imaging phantom design

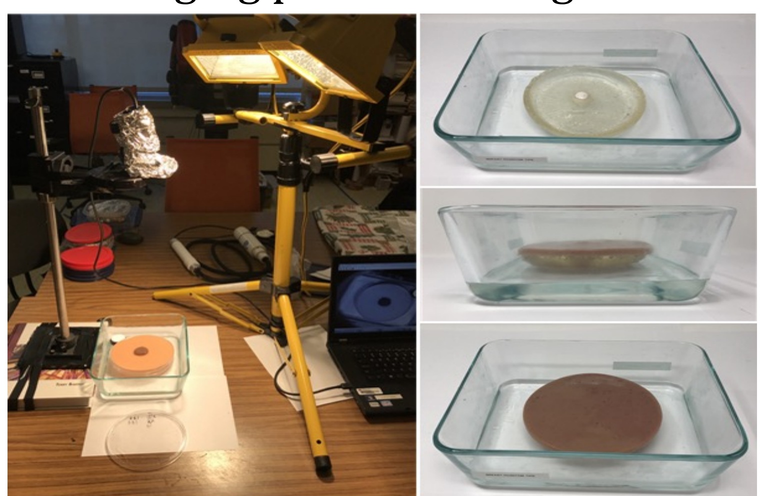


Figure : Bimodal imaging phantom implementation

Multimodal Index – Results

Table : Multimodal Index Results

TPD Sample	MPD Sample	Tactile Index	Spectral Index	Multimodal Index
1 shallow	1	0.62	0.01	0.19
2 shallow	2	0.31	0.59	0.51
3 shallow	3	0.70	0.63	0.65
4 shallow	4	0.54	0.20	0.30
5 shallow	5	0.70	0.41	0.50
6 shallow	6	0.41	0.97	0.80
1 deep	1	0.50	0.01	0.15
2 deep	2	0.65	0.59	0.61
3 deep	3	0.72	0.63	0.66
4 deep	4	0.42	0.20	0.27
5 deep	5	0.73	0.41	0.51
6 deep	6	0.47	0.97	0.82

Note: The darker is the gray color of a cell in the Multimodal Index results column, the higher mimicked cancer probability is for that case. The white colored cells in the last column indicate mimicked benign cases. The dark gray colored cells show mimicked malignant cases.

Conclusions

- We developed the **bimodal imaging system** and its calculation **algorithms** to capture tactile and multispectral properties of breast tumors and tissues.

- We explained the novel **Profile Diagrams** method

  We capture, encode, and analyze tactile and multispectral imaging signals as pattern images in the application meaningful way.

- In **TIP experiments**, we classified tumors based on depth, size, and stiffness using TPDs and CNN. We also quantified the size and stiffness of tumors.

  TIP can be used to differentiate malignant from benign tumors.

- In **MIP experiments**, we classified superficial breast tissues based on asymmetry, texture, and inflammation factors using MPDs and CNN.

  MIP can help screening for inflammatory breast cancer.

- We developed the method to calculate the individualized **Multimodal Index** for patients based on the imaging data from TIP and MIP modalities, and the individual breast cancer risk.

Thank you!